

## FENT COOPERATION TREA

PCT

NOTIFICATION OF ELECTION  
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C.20231  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 13 September 2000 (13.09.00)	To:  Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE  in its capacity as elected Office
International application No. PCT/US00/01350	Applicant's or agent's file reference 062308.0351
International filing date (day/month/year) 21 January 2000 (21.01.00)	Priority date (day/month/year) 22 January 1999 (22.01.99)
Applicant  MORSEMAN, John, P. et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

19 August 2000 (19.08.00)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  S. Mafla  Telephone No.: (41-22) 338.83.38
---	--

## INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 00/01350

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 G01N33/532

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	P. DAGENAIS ET AL.: "Direct covalent attachment of small peptide antigens to enzyme-linked immunosorbent assay plates using radiation and carbodiimide activation." ANALYTICAL BIOCHEMISTRY., vol. 222, no. 1, October 1994 (1994-10), pages 149-155, XP002138318 ACADEMIC PRESS INC. NEW YORK., US ISSN: 0003-2697 cited in the application the whole document --- -/-	1-7

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

22 May 2000

29/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Griffith, G

## INTERNATIONAL SEARCH REPORT

National Application No

PCT/US 00/01350

-1-

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	M. R. LEWIS ET AL.: "A facile, water-soluble method for modification of proteins with DOTA. Use of elevated temperature and optimized pH to achieve high specific activity and high chelate stability in radiolabeled immunoconjugates." BIOCONJUGATE CHEMISTRY., vol. 5, no. 6, 1994, pages 565-576, XP002138319 AMERICAN CHEMICAL SOCIETY, WASHINGTON., US ISSN: 1043-1802 the whole document ---	1-7
A	M. K. GHOSH ET AL.: "Preparation and characterization of methotrexate-immunoglobulin conjugates." DRUG DESIGN AND DELIVERY., vol. 4, no. 1, 1989, pages 13-25, XP000910702 HARWOOD ACADEMIC PUBLISHERS GMBH., XX the whole document ---	1-7
A	CHEMICAL ABSTRACTS, vol. 113, no. 21, 19 November 1990 (1990-11-19) Columbus, Ohio, US; abstract no. 187238, Z. HAN ET AL.: "Covalent coupling of papain and N-hydroxysuccinimide esters of crosslinked agarose." page 325; column 2; XP002138321 abstract & SHENGWU GONGCHENG XUEBAO, vol. 6, no. 1, 1990, pages 76-80, ---	1-7
A	WO 97 27885 A (J. M. LEE) 7 August 1997 (1997-08-07) ----	

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

national Application No

PCT/US 00/01350

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9727885 A	07-08-1997	CA 2168283 A	30-07-1997	AU 1434097 A 22-08-1997

REC'D 02 OCT 2000  
WIPO PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference  001986woHPg	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.  PCT/US00/01350	International filing date (day/month/year)  21/01/2000	Priority date (day/month/year)  22/01/1999	
International Patent Classification (IPC) or national classification and IPC  G01N33/532			
Applicant  MARTEK BIOSCIENCES CORPORATION			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

Date of submission of the demand  19/08/2000	Date of completion of this report  30.10.2000
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Moreno de Vega, C Telephone No. +49 89 2399 7486
	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/01350

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-26                   as originally filed

**Claims, No.:**

1-7                   as originally filed

**Drawings, sheets:**

1/2-2/2               as originally filed

2. The amendments have resulted in the cancellation of:

the description,       pages:  
 the claims,           Nos.:  
 the drawings,         sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/01350

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims 1-7
	No:	Claims
Inventive step (IS)	Yes:	Claims 1-7
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-7
	No:	Claims

**2. Citations and explanations**

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/01350

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Novelty (Article 33(2) PCT)**

Claims 1-7 meet the requirements as set forth in Article 33(2) PCT. None of the documents of the known prior art discloses a single vessel containing N-hydroxysuccinimide (NHS), a carbodiimide and a label containing an amine or a carboxyl moiety, these components in a dry form suitable for rehydration (claim 1), a single vessel containing a label and an activating reagent in dry form for rehydration (claim 7), and methods for conjugating a label to target moieties using the said reagent vessels.

**2. Inventive step (Article 33(3) PCT)**

The technical problem to be solved by present claims 1-7 is the provision of simplified methods for coupling labels to particular target moieties, avoiding uncontrolled reactions which produce unwanted side-products. The solution provided by these claims, namely the use of NHS chemistry in an "one tube" format, in which all reactants are prepared separately and combined in such a way that they do not react with each other until the targeted compound is added to activate the cross-linking chemicals. This solution is neither suggested nor disclosed in the known prior art. Thus, claims 1-7 meet the requirements of Article 33(3) PCT.

**Re Item VII**

**Certain defects in the international application**

It seems that in claims 5 and 7, instead of "activating reagent" it should read "activating reagent".

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/01350

**Re Item VIII**

**Certain observations on the international application**

The term "about" used in claim 1 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).

## PENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>062308.0351</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/01350</b>	International filing date ( <i>day/month/year</i> ) <b>21/01/2000</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>22/01/1999</b>
Applicant <b>MARTEK BIOSCIENCES CORPORATION et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of Invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

1

None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/01350

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 G01N33/532

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>P. DAGENAIS ET AL.: "Direct covalent attachment of small peptide antigens to enzyme-linked immunosorbent assay plates using radiation and carbodiimide activation."  <b>ANALYTICAL BIOCHEMISTRY</b>,          vol. 222, no. 1, October 1994 (1994-10),          pages 149-155, XP002138318          ACADEMIC PRESS INC. NEW YORK., US          ISSN: 0003-2697          cited in the application          the whole document</p> <p>---</p> <p style="text-align: center;">-/--</p>	1-7

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

22 May 2000

Date of mailing of the international search report

29/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Griffith, G

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/01350

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	M. R. LEWIS ET AL.: "A facile, water-soluble method for modification of proteins with DOTA. Use of elevated temperature and optimized pH to achieve high specific activity and high chelate stability in radiolabeled immunoconjugates." BIOCONJUGATE CHEMISTRY., vol. 5, no. 6, 1994, pages 565-576, XP002138319 AMERICAN CHEMICAL SOCIETY, WASHINGTON., US ISSN: 1043-1802 the whole document ---	1-7
A	M. K. GHOSH ET AL.: "Preparation and characterization of methotrexate-immunoglobulin conjugates." DRUG DESIGN AND DELIVERY., vol. 4, no. 1, 1989, pages 13-25, XP000910702 HARWOOD ACADEMIC PUBLISHERS GMBH., XX the whole document ---	1-7
A	CHEMICAL ABSTRACTS, vol. 113, no. 21, 19 November 1990 (1990-11-19) Columbus, Ohio, US; abstract no. 187238, Z. HAN ET AL.: "Covalent coupling of papain and N-hydroxysuccinimide esters of crosslinked agarose." page 325; column 2; XP002138321 abstract & SHENGWU GONGCHENG XUEBAO, vol. 6, no. 1, 1990, pages 76-80, ---	1-7
A	WO 97 27885 A (J. M. LEE) 7 August 1997 (1997-08-07) ----	

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 00/01350

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9727885 A	07-08-1997	CA 2168283 A AU 1434097 A	30-07-1997 22-08-1997

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						